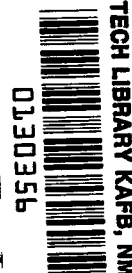


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# ON THE DYNAMICS OF CAPILLARIES AND THE EXISTENCE OF PLASMA FLOW IN THE PERICAPILLARY LYMPH SPACE

*by John T. Howe and Yvonne S. Sheaffer*

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NATIONAL AERONAUTICS AND SPACE ADMINISTRATION

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ON THE DYNAMICS OF CAPILLARIES AND THE EXISTENCE OF  
PLASMA FLOW IN THE PERICAPILLARY LYMPH SPACE<sup>1</sup>

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SUMMARY

In 1958, Sapirstein proposed that the surplus plasma associated with low organ hematocrits resides in an external annulus about the capillary endothelium. This hypothesis was based on observations of such an annulus by Heimberger in 1926 (although Heimberger supposed the annulus to be filled with lymph). The pericapillary space has since been observed by Gibson, Bosley, and Griffiths (1956) and Ehrling (1964). Sapirstein suggested that the capillary endothelium is not a real barrier to macromolecules; instead, the "true hematolymph barrier" is actually the outer wall of the Heimberger annulus. The present paper describes the results of an analysis of this double-walled capillary model from the hydrodynamic point of view.

The hydrodynamic analysis shows that even without the annulus, one can account for organ hematocrits as low as 50 percent of the large blood vessel hematocrits. But the corresponding pressure gradients fall outside the range of those cited in the literature. Moreover, without the plasma annulus one cannot readily account for those hematocrit ratios below 0.5 (actually as low as 0.35) that have been observed experimentally. However, the analysis shows that with the annulus of plasma, hematocrit ratios as low as 0.27 can be explained, and the corresponding pressure gradients fall within the range cited in the literature.

Although the annulus of plasma was proposed by Sapirstein to explain the surplus of plasma in some organs, it (surprisingly) allows a deficit of plasma under some circumstances. The explanation lies in the dynamics. The analysis shows that for this condition the endothelium radius is only slightly larger than that of the red cells. Thus the pressure gradient can drive plasma against the low resistance of the annulus (and on to the large vessels) at a greater rate than it can drive cells along inside the endothelium because of the snug fit.

INTRODUCTION

In 1926, Heimberger (ref. 1) observed that intradermal gas produced electrolytically (by use of a fine needle introduced through the skin) forms a large gas bubble in the surrounding tissue. But if the needle is brought close to a capillary wall, the picture changes suddenly to an enormous number of very small bubbles, which form a veil all around and along the capillary. From the veil, branches sometimes go to other capillaries or end somewhere

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<sup>1</sup>This paper was presented at the International Symposium on the Human Capillary Circulation, Jamaica, 1966.

within the tissue. He noted that the shape of the capillary is surprisingly unaffected by the bubbles. From this experiment, he suggested that a pericapillary lymph space exists all along and all around a capillary.

Further anatomical evidence of a pericapillary space has been obtained photomicrographically in the human nailfold in vivo by Bosley (ref. 2) and his associates.

The Heimberger concept of the pericapillary lymph space was drastically modified by Sapirstein (ref. 3) in 1958 to account for organ hematocrits that are much lower than the large blood vessel hematocrits. In the rat, he found excess plasma in every organ and concluded that wherever a vascular bed exists there is excess plasma. Sapirstein argued that the annular space around capillaries observed by Heimberger does not contain lymph at all, but rather, plasma, and inferred the existence of such capillaries in other organs. He postulated that the old capillary endothelium is confining for red cells only, the plasma outside the endothelium being quite accessible to macromolecules. Thus he suggests that the real barrier, across which Starling's hypothesis is made manifest, is a second membrane between the pericapillary lymph (which is really plasma) and the true lymphatic.

The excess plasma in some organs has been observed and explained in a different way by others. Pappenheimer and Kinter (ref. 4) studied the hematocrit of the mammalian kidney and proposed a theory to account for the excess plasma in the organ. It supposes that incoming plasma and cells are progressively separated by plasma skimming, and that cell-rich blood passes through a short circulation while the plasma passes through a long circulation in the capillary network. That is, cells pass through the organ more rapidly than does plasma. The suggestion is that they both move at comparable velocities, but over different distances.

The Pappenheimer-Kinter theory says that the excess plasma in the organ is explainable only in terms of the aggregate of flows from all the vessels of the organ. But the theory suffers from the fact that plasma skimming actually occurs at random rather than in the systematic way required by the model. On the other hand, the Sapirstein viewpoint carried to its limit would be that the excess plasma in the organ is explainable in terms of the flow in any single capillary; the capillaries in a bed have a common hematocrit - that of the organ. In the first theory, plasma skimming plays a dominant role. In the second, its effect on organ hematocrit is small.

Goresky (ref. 5) in a recent two-compartment model of the microcirculation of the liver uses an extravascular space readily accessible to plasma, but not to cells. He assumes that the extravascular plasma is at rest. We shall see as a consequence of the present analysis that for low hematocrit ratios that occur in the liver, the pericapillary plasma may be almost at rest - but not quite.

In this paper, we shall examine the Heimberger-Sapirstein model of the capillary. If we are to believe the anatomical evidence, the fluid annulus about the endothelium exists, at least near the skin. Since the endothelium is permeable to water, plasma has access to the annulus. The question is, to

what extent? To the extent that there is an important axial flow of plasma in the annulus that is driven by the same axial pressure gradient as the flow of cells and plasma within the endothelium? And since we will carry the Sapirstein viewpoint to its limit, what of the heterogeneity of the capillary bed? Can the capillaries have a common hematocrit and still have different diameters, cell spacings, and cell velocities?

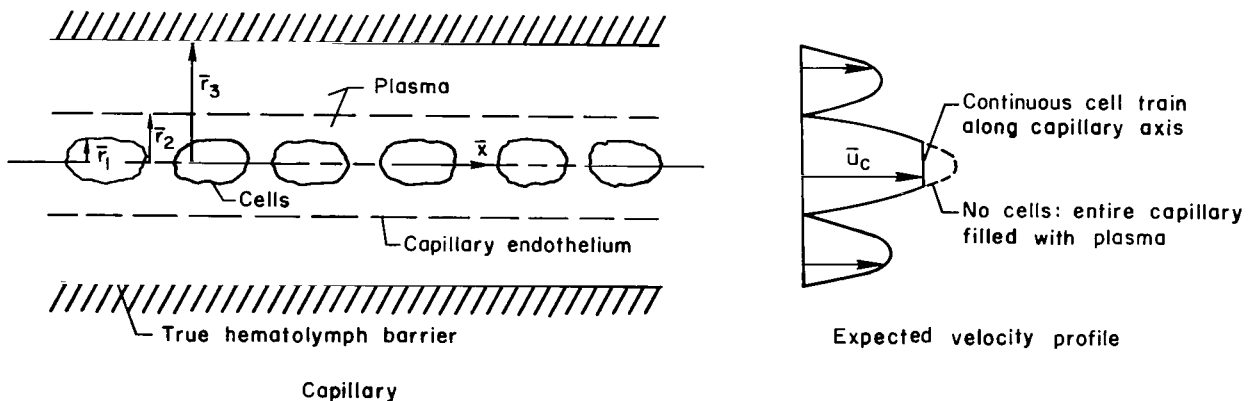
We approach this problem from the hydrodynamic point of view. The hydrodynamic analysis will lead to a prediction of the radii of both the endothelium and the outer "true hematoymph barrier" of Sapirstein as a function of hematocrits. It will yield velocity profiles across the capillary and will give a useful linear relationship between cell speed and pressure gradient.

It will be shown that even without the annulus, one can account for organ hematocrits that are as low as 50 percent of the large blood vessel hematocrits on the basis of flow in a single capillary. No "mechanisms" are needed, no short path for cells nor long path for plasma; but without the plasma annulus, one cannot readily account for those hematocrit ratios below 0.5 (actually as low as 0.35) that have been observed experimentally. The analysis shows, however, that with the annulus of plasma, hematocrit ratios as low as 0.27 can be explained.

Although the annulus of plasma was proposed by Sapirstein to explain the surplus of plasma found in some organs, it (surprisingly) also allows a deficit of plasma under some conditions. The simple explanation will be revealed by the dynamics. Moreover, a capillary having a hematocrit higher than that of the large blood vessel (plasma deficit) will be shown to have a special characteristic which quite possibly is observable experimentally. In general, the analysis will show what experimental observables should be measured in a given organ to give a conclusive answer about the existence of a flow of plasma in the lymph space.

## ANALYSIS

The model of the capillary is shown on the left in sketch (a). The radius



Sketch (a)

of erythrocytes is designated by  $\bar{r}_1$ ; the (as yet) unknown radius of the endothelium is  $\bar{r}_2$ ; and the (as yet) unknown radius of the true barrier between pericapillary plasma and the true lymphatic is  $\bar{r}_3$ .

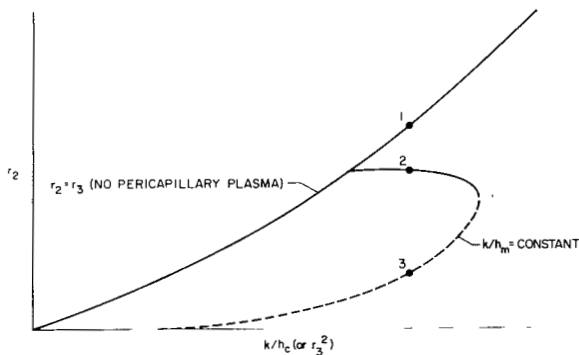
The mathematical details of the hydrodynamic analysis of the blood flow through this capillary model are presented in the appendix, along with an evaluation of the model. Briefly, the principles of momentum and mass conservation as set forth in any standard work on hydrodynamics (ref. 6) are employed. Solutions of the momentum equation yield expressions for the velocity profiles across the capillary (shown schematically on the right in sketch (a)). These profiles are used in mass conservation expressions written in terms of the large vessel hematocrit,  $h_m$ , the organ hematocrit,  $h_c$ , and the fraction of the cell train that is actually cells,  $k$ . The result is a fourth degree expression relating these quantities to  $r_2$  (the endothelium radius normalized with respect to cell radius,  $\bar{r}_1$ ). Thus our results and conclusions will be obtained by studying the roots of this relatively simple algebraic expression,

$$\left[ \left( \frac{k}{h_c} \right)^2 - r_2^2 - (r_2^2 - 1) \left( \frac{2k}{h_m} - 1 \right) \right] \ln \left( \frac{\sqrt{k/h_c}}{r_2} \right) = \left( \frac{k}{h_c} - r_2^2 \right)^2 \quad (1)$$

## DISCUSSION OF RESULTS

### Capillary Radii, Hematocrits, and Associated Quantities

Numerical solutions of equation (1) show that for a given  $k/h_c$  there are typically three kinds of roots numbered 1, 2, and 3 in sketch (b). The first



Sketch (b)

of these has no pericapillary plasma ( $r_2 = r_3$ ). The other two roots, 2 and 3, do have pericapillary plasma ( $r_2$  is less than  $r_3$ ). They form a pair of roots having a common value of  $k/h_m$ . We will refer to root 2 as lying on the upper branch of the root having pericapillary plasma (solid line) and root 3 as lying on the lower branch of the root having pericapillary plasma (dashed line in sketch (b)). In figure 1, we show a family of such roots having pericapillary plasma (each root characterized by a given  $k/h_m$ ). The overlay of light lines of constant  $h_c/h_m$  will be discussed subsequently.

Now let us examine roots without and with pericapillary plasma separately.

### Roots With No Plasma Outside the Endothelium

Unlike the roots having plasma outside the endothelium, this root (the upper curve in fig. 1) is not characterized by a single value of  $k/h_m$ .

Instead, there is a different value  $k/h_m$  for every point along the root. By use of equations (A10), (A12), (A7), (A8), and (A5) the relationship between  $k/h_c$  and  $k/h_m$  for this root is readily found to be

$$\frac{k}{h_c} + 1 = 2 \frac{k}{h_m} \quad (2)$$

If the large vessel hematocrit is 0.4, the maximum value that  $k/h_c$  can have is 4, and figure 1 shows that the maximum radius of the endothelium is twice the cell radius. At this maximum  $k/h_c$ , it is clear that the capillary hematocrit must not exceed 0.25. This limit is not subject to the approximations made about bolus flow because it corresponds to  $k = 1$  (full cylindrical train) for which the analysis should be strictly correct. At values of  $k/h_c$  less than the maximum,  $k$  will be less than unity, and  $h_c$  will be greater than 0.25 (with  $h_m$  still 0.4) as shown in figure 2.

We may note in figure 2 that the maximum value of  $h_c/h_m$  is unity. By use of equation (2) rewritten as

$$\frac{h_c}{h_m} = \frac{1}{2} \left( 1 + \frac{h_c}{k} \right) \quad (3)$$

and the fact that  $k/h_c \geq 1$ , it is easy to see that, generally, a vascular bed hematocrit larger than the large blood vessel hematocrit cannot be reconciled by use of a capillary that does not have an active flow of excess plasma outside the endothelium. However, we shall see subsequently that a portion of each root having extra plasma outside the endothelium does allow the capillary hematocrit to exceed that of the large vessels.

#### Roots With Plasma Outside the Endothelium

For a given  $k/h_m$ , there are two branches of these roots. The upper branch corresponds to large endothelium radii relative to those of the lower branch as can be seen in figure 1. Roots are shown for values of  $k/h_m$  between 2.5 and 1.25. These values cover a range of practical interest. For example, if the large vessel hematocrit is 0.4,  $k/h_m = 2.5$  means that  $k = 1$ , which corresponds to a full train of cells moving along the capillary axis; and  $k/h_m = 1.25$  means that  $k = 1/2$ , which corresponds to every other cell in the train being missing and its space filled with plasma.

For a given  $k/h_m$ , figure 1 shows a maximum allowable value of  $k/h_c$  for these roots. The maxima are presented graphically in figure 3. These maxima relate importantly to the question of existence of the annulus of plasma about the endothelium as follows. The maximum allowable value of  $k/h_c$  at a given value of  $k/h_m$  means that there is a minimum value of  $h_c/h_m$ ,

$$\left( \frac{h_c}{h_m} \right)_{\min} = \frac{k/h_m}{(k/h_c)_{\max}} \quad (4)$$

which is shown graphically by the lower curve in figure 4. For comparison, the ratio  $h_c/h_m$  for a capillary that has no annulus of plasma outside the endothelium is a single-valued function of  $h_m/k$  as can be seen by rewriting

equation (2) to yield

$$\frac{h_c}{h_m} = \frac{1}{2 - h_m/k} \quad (5)$$

which is shown by the upper curve in figure 4. Here we have an interesting result. Without the annulus of plasma outside the endothelium, the lowest possible value of  $h_c/h_m$  is 0.5. If  $h_m = 0.4$  (a typical value for humans), the minimum possible ratio is raised to 0.625. Sapirstein lists values of that ratio as low as 0.44 and 0.46 for the liver and kidney of the rat, and reference 4 lists 0.35 for the kidney of the dog. The figure shows that such low ratios (actually as low as 0.27) can be reconciled on the basis of a single capillary only if the annulus of plasma exists outside the endothelium. It is important to note that this result has not been significantly influenced by the approximations of the model analyzed. That is, the minimum  $h_c/h_m$  for a given  $h_m$  occurs when  $k = 1$  (which is easily deduced from fig. 4, and is seen in fig. 2). This corresponds to a full train of cells, which is our model at its best.

We turn attention now to the problem of vascular hematocrits larger than those of large blood vessels (deficit of plasma in organ). It is easy to see in figure 1 that any root for which  $h_c/h_m \geq 1$  must lie below the line  $h_c/h_m = 1$  at the bottom of the figure. For  $k/h_m \leq 2.5$ , the root corresponds to a capillary whose endothelium radius is, at the most, 5 percent larger than the cell radius. The radius of the true hematolymph barrier is, at the most, 60 percent larger than the cell radius. A mechanism for the deficit of plasma in the organ relative to the large blood vessels is at once apparent from the dynamics. That is, the pressure gradient will drive plasma along the wide annulus between endothelium and true barrier at a higher velocity than it can drive cells along inside the endothelium because the close clearance between the cell and the endothelium offers so much fluid resistance. Thus the relative excess of plasma in the large blood vessel can be supplied by plasma that moves more rapidly through the space outside the endothelium than the cells move along inside the endothelium, which will subsequently be shown quantitatively (e.g., in the profile  $k/h_c = 2$  in fig. 7(a)). That is the means for reconciling such hematocrits by use of a single capillary having a double wall.

#### Heterogeneity of the Capillary Bed

A comparison of the two capillary models on the basis of a capillary bed leads to an interesting result. If there is no annulus of plasma,  $r_2 = r_3$  and equations (A12) and (3) yield

$$\frac{h_c}{h_m} = \frac{1}{2} \left( 1 + \frac{1}{r_2^2} \right) \quad (6)$$

Thus, for a given  $h_c/h_m$  there is one value of  $r_2$  and, from equation (5), there is one value of  $k/h_m$ . If  $h_m$  is fixed, there is one value of  $k$ . This means that if we are to reconcile a capillary bed hematocrit  $h_c$  to a large blood vessel hematocrit  $h_m$  on the basis of flow in a single capillary, all the capillaries in the bed must have the same diameter and the same cell



spacing, provided there is no annulus of plasma about the endothelium. But experiments show that the sizes and cell spacings differ among neighboring capillaries (ref. 7).

However, a capillary bed with an annulus of plasma about the endothelium has no such restriction, as illustrated by the family of light lines in figure 1. Each line is the locus of points which have a fixed  $h_c/h_m$ ; if we view  $h_m$  as fixed, then  $h_c$  is constant all along the line. The abscissa shows, however, that  $k/h_c$  varies along a light line and thus  $k$  varies, and, of course, both  $r_2$  and  $r_3$  vary; that is, we can reconcile a capillary bed hematocrit  $h_c$  to a large blood vessel hematocrit  $h_m$  on the basis of the flow in a single capillary, and the capillaries in the bed can be different sizes and carry different flows with different cell spacings. All such capillaries have the same hematocrit  $h_c$ . The annulus of plasma about the endothelium is all that is needed to make this possible.

To this point, we have not needed to consider pressure gradients or cell speed quantitatively. Indeed, the results are independent of specific values of these quantities.

#### Cell Speed and Pressure Gradient

We may compare our theoretical results with existing experimental results to assess how reasonable the pericapillary plasma model is. Ideally, we should have simultaneous experimental measurements of cell speed and spacing, pressure drop from one end of the capillary to the other, large blood vessel hematocrit, and the hematocrit of the vascular bed<sup>2</sup> so that we can compare item by item. However, simultaneous measurements are available only for the two hematocrits. Although capillary pressure drops or pressure gradients are mentioned in the literature (refs. 10-20), they are not associated with any  $k/h_c$ . Thus we simply represent the values obtained from the references as tick marks along the ordinate of figure 5.<sup>3</sup> The cell velocity associated with the pressure drops in dogs was cited (refs. 12 and 13) as 0.5 and 0.4 mm/sec (the former being derived from observations on capillaries in regions showing a brisk blood flow), but was not mentioned elsewhere. However, Bard noted that the average rate of flow in the systemic capillaries of the human body at rest is far below the 0.5 mm/sec (ref. 12). Best and Taylor (ref. 11) presented a graph for pressure drop in human skin capillaries (p. 163) and listed a cell speed of 0.5 mm/sec for resting dogs (p. 176).

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<sup>2</sup>Such measurements are not unreasonable. For example, cell speed and spacing should be readily measurable from motion pictures (such as those obtained by Nicoll and Webb (ref. 8)) of cells moving through capillaries in a bat's wing or in a webbed foot. Pressure drop could possibly be measured at the same time by a technique such as Landis (ref. 9) used on the skin of the hand, and finally, large blood vessel and vascular bed hematocrits could be obtained from the specimen.

<sup>3</sup>Where pressure drops are cited in the literature, we have calculated pressure gradients by associating the pressure drops with capillaries 0.4 mm long (100 cell radii long approximately).

The theoretical pressure gradients corresponding to the various roots of  $r_2$  are plotted as heavy, solid or broken lines in figure 5 for a cell speed of 0.4 mm/sec. (A similar plot for another cell speed could be obtained simply by shifting the ordinate scale, because the pressure gradient is simply proportional to cell speed (eq. (A5).) It is seen that the lowest pressure gradient for a given  $k/h_c$  is associated with the root which has no pericapillary plasma. For each root having pericapillary plasma, the upper branch (defined by sketch (b) and fig. 1) has a lower pressure gradient than the lower branch. Loci of constant  $h_c/h_m$  have been overlaid (light lines) in figure 5.

A comparison of the pressure gradients cited in the literature with that corresponding to the root for no pericapillary plasma leads to the following argument. (1) For a cell speed of 0.4 mm/sec and a pressure gradient not less than  $4 \times 10^4$  dynes/cm<sup>3</sup> (the lowest cited), the ratio  $k/h_c$  for the capillary without the annulus of plasma about the endothelium is between 1.5 and 1 according to the figure. (2) The corresponding range of  $h_c/h_m$  from equation (3) is 0.833 to 1. (3) If the organ hematocrit is to be less than 83 percent of the large blood vessel hematocrit, we must have an annulus of plasma about the endothelium in order to reconcile the hematocrits on the basis of flow in a single capillary. (4) If cell speed is indeed much less than 0.4 mm/sec (ref. 12), organ hematocrits must be essentially the same as large blood vessel hematocrits unless there is a plasma annulus outside the endothelium.

On the other hand, if we allow the annulus of flowing plasma, the minimum pressure gradient cited in the literature ( $4 \times 10^4$  dynes/cm<sup>3</sup>) can be achieved by a range of cell spacings and hematocrits. More importantly, the annulus allows many ratios of  $h_c/h_m$  which are much lower than the 0.833 mentioned above. For example, if  $k/h_m$  is 1.875, we see that  $k/h_c$  is 3.5 for that pressure gradient, for which the ratio  $h_c/h_m$  is 0.536, a very agreeable number in the light of Sapirstein's data. This ratio is still not the minimum allowed at that pressure gradient. (We estimate that the minimum for this case is about 0.5.)

Thus the comparison of the theoretical result with existing pressure data favors the existence of the annulus of plasma outside the endothelium.

The comparison between the single-walled capillary and double-walled capillary can be restated more generally. That is, given one of the quantities  $r_2$ ,  $k/h_c$ , and  $k/h_m$ , the sleeveless capillary has no choice of the other two, but the capillary having an extra sleeve of plasma can have any number of combinations of the other two. If, in addition, either  $\bar{u}_c$  or  $d\bar{p}/d\bar{x}$  is specified, the sleeveless capillary has no choice of the other one, but the capillary having the extra sleeve of plasma can have a range of values of the other. Thus, capillaries having an annulus of plasma outside the endothelium can accommodate blood flows over a much wider range of conditions than can sleeveless capillaries. This argues in favor of the existence of plasma in the pericapillary lymph space.

## Blood Velocity Profiles

The velocity profiles across the capillary, normalized with respect to cell velocity, are shown in figures 6, 7, and 8 corresponding to the three roots,  $r_2$ , of equation (1) shown in figure 1. Velocity profiles for the root having no pericapillary plasma ( $r_2 = r_3$ ) are shown in figure 6.

The velocity profiles corresponding to the lower branch of the roots in figure 1 having pericapillary plasma are shown in figure 7(a) for  $k/h_m = 2.5$  and in figure 7(b) for  $k/h_m = 1.25$ . A typical overall profile is shown by the heavy line in figure 7(a).

The profile for  $k/h_c = 2$  in that figure is of special interest in that it corresponds to a capillary hematocrit greater than that for the large blood vessel (by a factor 1.25). The maximum plasma velocity for that case occurs in the annulus outside the endothelium and is almost twice the cell velocity. For  $h_c/h_m = 1.5$ , the corresponding maximum plasma speed would be about 3.5 times that of the cell speed. In such a capillary, the difference between the transit times of labeled plasma and labeled cells would quite likely be observable experimentally.

The velocity profiles with pericapillary plasma, corresponding to the upper branch of the roots in figure 1, are shown in figure 8(a) for  $k/h_m = 2.5$  and in figure 8(b) for  $k/h_m = 1.25$ . For  $k/h_m = 2.5$ , the maximum  $k/h_c$  is 6.92 (fig. 1), so the profile for  $k/h_c = 6.92$  in figure 8(a) actually pertains to the lower root as well and could have appeared in figure 7(a). Similarly, for  $k/h_m = 1.25$ , the profile for  $k/h_c = 2.16$  in figure 8(b) is applicable to figure 7(b) as well. The interesting feature of the upper branch roots is that the pericapillary plasma moves very slowly. There is a marked contrast in pericapillary plasma velocities between the upper and lower roots for a given  $k/h_m$  and  $k/h_c$ . In particular, for  $k/h_m = 2.5$  and  $k/h_c = 5$ , the upper root (fig. 8(a)) shows a maximum velocity in the pericapillary plasma of only 1 percent of the cell speed, while that of the lower root (not actually shown in fig. 7(a)) is 120 percent of the cell speed. This suggests that after labeled plasma enters the capillary, the length of time required for the concentration of labeled plasma leaving the capillary to become constant will be governed by the pericapillary plasma speed. The time may be of the order of 100 times cell transit time and thus may be observable experimentally.

## CONCLUSIONS

The results of this approximate analysis of the dynamics of the capillary and plasma-filled pericapillary lymph annulus suggest a number of qualitative properties and lead to a number of quantitative conclusions about capillaries, which may be stated briefly as follows.

For a given pressure gradient, the cell velocity of a train of cells moving along the axis of a capillary is less than the maximum parabolic velocity (Poiseuille flow) that plasma alone passing through the capillary would

have. Thus for a train of cells passing through the capillary such that the cells are not butted against one another end to end but are instead separated by a cylinder of plasma, there is a defect in cell speed, or more importantly, a defect in mass flux, relative to that of Poiseuille flow of plasma. This defect is likely to be the cause of bolus flow, a doughnut-shaped vortex in the plasma between cells.

The analysis predicts a linear relationship between the pressure gradient and volume rate of flow of whole blood in the capillary. This theoretical result is in agreement with results of previous experiments on the flow of whole blood in glass tubes of capillary diameter.

We have explored the point of view that the organ hematocrit can be reconciled with the large blood vessel hematocrit on the basis of flow in any single capillary; that is, the organ hematocrit is essentially the same as the capillary hematocrit. Although ratios of organ hematocrit to large blood vessel hematocrit of less than 1 have been explained by plasma traveling a long path and cells traveling a short path through an organ, we have shown that ratios between 0.5 and 1 (but not greater than 1) can be accounted for even if plasma and cells travel the same distance through a common capillary without an annulus of flowing plasma outside the endothelium. But only those capillary pressure gradients for ratios of hematocrits above 0.83 agree with those cited in the literature. Moreover, without the plasma annulus one cannot readily account for those ratios of hematocrits below 0.5 (actually as low as 0.35) that have been observed experimentally. However, the analysis shows that with the annulus of plasma, ratios as low as 0.27 can be explained. The pressure gradients for ratios of hematocrits above 0.5 fall within the range cited in the literature.

Although the annulus of plasma was proposed by Sapirstein to explain the surplus of plasma found in all organs except the spleen, it (surprisingly) could also explain a deficit of plasma under some conditions. That is, the annulus also allows high ratios of hematocrits. The explanation lies in the dynamics. The analysis shows for this condition that the endothelium radius is only slightly larger than that of the red cells. Thus the pressure gradient can drive plasma against the low resistance of the annulus (and on to the large vessels) at a greater rate than it can drive cells along inside the endothelium because of the snug fit. Because of the velocity difference, labeled plasma should be observed to pass through the capillary more rapidly than the labeled cells.

In general, it was shown that the existence of a flow of plasma in an annulus about the endothelium is advantageous in broadening the range of flow conditions that can be accommodated by a single capillary.

With reference to specific organs, the analysis shows that the ratio (as cited in the literature) of organ hematocrit to large blood vessel hematocrit for the heart, lungs, brain, gut, and carcass can be explained on a single

capillary basis with or without the pericapillary plasma. But the ratio for liver and kidney can be explained on a single capillary basis only with the pericapillary plasma.

Ames Research Center  
National Aeronautics and Space Administration  
Moffett Field, Calif., April 26, 1966

## APPENDIX A

### HYDRODYNAMIC ANALYSIS

#### SYMBOLS

$h_c$	dynamic hematocrit of capillary or organ
$h_m$	bulk hematocrit (in general), or (if average cell speed equals average blood speed in large vessel) dynamic hematocrit of large blood vessel
$k$	fraction of cells present in a train of cells
$\bar{p}$	pressure
$Q_{jk}$	mass rate of flow in annulus between radii $\bar{r}_j$ and $\bar{r}_k$
$r$	dimensionless radius; $\bar{r}/\bar{r}_1$
$\bar{r}$	radius
$\bar{r}_1$	radius of cell as it moves through endothelium ( $0.4 \mu$ )
$\bar{r}_2$	radius of endothelium
$\bar{r}_3$	radius of true hematolymph barrier
$\bar{u}$	velocity parallel to capillary axis
$\bar{u}_c$	velocity of cells
$\bar{x}$	distance from capillary entrance measured along capillary axis
$\bar{\mu}$	viscosity coefficient of plasma (1.9 cp. at $23.5^\circ \text{C}$ )
$\bar{\rho}$	mass density

#### CAPILLARY MODEL

The model of the capillary that we studied was shown in sketch (a).

Specifically, our model is that of a continuous train of cells moving along the axis of a coaxial capillary. When cells in the train are missing, we simply assume that their space is filled with plasma which moves along with the train without changing the velocity. Some of the advantages and disadvantages of this model are discussed subsequently.

## MOMENTUM EQUATION

The ordinary differential equation expressing the conservation of momentum for a small fluid element of plasma flowing steadily parallel to the capillary axis  $\bar{x}$  is

$$\bar{\mu} \frac{d\bar{u}^2}{d\bar{r}^2} + \frac{\bar{\mu}}{\bar{r}} \frac{d\bar{u}}{d\bar{r}} - \frac{d\bar{p}}{d\bar{x}} = 0 \quad (A1)$$

Consideration of a balance of forces on a cylindrical train of cells moving at uniform velocity  $\bar{u}_c$  leads to the relation

$$\frac{\bar{r}_1}{2} \frac{d\bar{p}}{d\bar{x}} = \left( \bar{\mu} \frac{d\bar{u}}{d\bar{r}} \right)_{\bar{r}=\bar{r}_1} \quad (A2)$$

Use of this expression and the no-slip boundary condition at each wall in the integration of equation (A1) leads to the velocity profile in each region. Thus the velocity profile for the plasma between the cells and the endothelium ( $\bar{r}_1 \leq \bar{r} \leq \bar{r}_2$ ) is

$$\bar{u} = - \frac{1}{4\bar{\mu}} \frac{d\bar{p}}{d\bar{x}} (\bar{r}_2^2 - \bar{r}^2) \quad (A3)$$

while that between the endothelium and the true barrier ( $\bar{r}_2 \leq \bar{r} \leq \bar{r}_3$ ) is

$$\bar{u} = \frac{1}{4\bar{\mu}} \frac{d\bar{p}}{d\bar{x}} \left[ (\bar{r}^2 - \bar{r}_2^2) + \frac{(\bar{r}_3^2 - \bar{r}_2^2)}{\ln(\bar{r}_2/\bar{r}_3)} \ln \left( \frac{\bar{r}}{\bar{r}_2} \right) \right] \quad (A4)$$

Note that  $\bar{u} = \bar{u}_c$  at  $\bar{r} = \bar{r}_1$  and equation (A3) yields a useful linear relationship between cell speed and pressure gradient

$$\bar{u}_c = - \frac{1}{4\bar{\mu}} \frac{d\bar{p}}{d\bar{x}} (\bar{r}_2^2 - \bar{r}_1^2) \quad (A5)$$

## MASS FLOW

In an annulus between any two radii,  $\bar{r}_j$  and  $\bar{r}_k$ , the rate of mass flow along the capillary is

$$Q_{jk} = 2\pi\bar{\rho} \int_{\bar{r}_j}^{\bar{r}_k} \bar{u}\bar{r} d\bar{r} \quad (A6)$$

Thus the mass-flow rate in the cell region ( $0 \leq r \leq r_1$ ) is

$$Q_{01} = \pi \bar{\rho} \bar{u}_c \bar{r}_1^2 \quad (A7)$$

The mass-flow rate of the plasma between cells and endothelium obtained by use of equations (A3) and (A6) is

$$Q_{12} = - \frac{\pi \bar{\rho}}{8 \bar{\mu}} \frac{d\bar{p}}{d\bar{x}} (\bar{r}_2^2 - \bar{r}_1^2)^2 \quad (A8)^1$$

while that between endothelium and true barrier obtained by equations (A4) and (A6) is

$$Q_{23} = - \frac{\pi \bar{\rho}}{8 \bar{\mu}} \frac{d\bar{p}}{d\bar{x}} (\bar{r}_3^2 - \bar{r}_2^2) \left\{ 2\bar{r}_3^2 - (\bar{r}_3^2 - \bar{r}_2^2) \left[ 1 + \frac{1}{\ln(\bar{r}_3/\bar{r}_2)} \right] \right\} \quad (A9)$$

The hematocrit of the large blood vessels feeding or fed by capillaries like this one is

$$h_m = \frac{k Q_{01}}{Q_{01} + Q_{12} + Q_{23}} \quad (A10)$$

where  $k$  is the fraction of the cell train cylinder that is actually cells. That is, if  $k = 1$ , the cells in the train are butted against one another; if  $k = 2/3$ , the cell train is two-thirds cells and one-third plasma.

Substituting equations (A7), (A8), and (A9) into (A10) leads to

$$\left[ \left( \frac{k}{h_c} \right)^2 - r_2^2 - (r_2^2 - 1) \left( \frac{2k}{h_m} - 1 \right) \right] \ln \left( \frac{\sqrt{k/h_c}}{r_2} \right) = \left( \frac{k}{h_c} - r_2^2 \right)^2 \quad (A11)$$

when we have noted that the capillary hematocrit is

$$h_c = k \frac{\bar{r}_1^2}{\bar{r}_3^2} \equiv \frac{k}{r_3^2} \quad (A12)$$

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<sup>1</sup>If equation (A5) is substituted into equation (A7) and the result added to equation (A8), an expression is obtained for the mass (or volume) rate of flow of whole blood within the endothelium as a linear function of pressure gradient. This linearity was one of the conclusions drawn from experiments (ref. 21) on whole blood flowing in glass tubes of capillary diameter. A linear relation between flow and pressure gradient also prevails for the capillary having an annulus of plasma about the endothelium as can be seen by adding equation (A9) to the above.



where the normalized radii  $r_2$  and  $r_3$  are

$$\left. \begin{aligned} r_2 &= \frac{\bar{r}_2}{\bar{r}_1} \\ r_3 &= \frac{\bar{r}_3}{\bar{r}_1} \end{aligned} \right\} \quad (A13)$$

Equation (A11) is the basic relationship employed in the text (eq. (1)). If we regard  $k/h_c$  and  $k/h_m$  as known, we at once know  $r_2$  from equation (A11) and  $r_3$  from equation (A12) (independent of any knowledge of pressure gradient and cell speed). Thus, if  $r_2$  is smaller than  $r_3$ , pericapillary plasma is necessary in order to satisfy mass and momentum conservation.

#### EVALUATION OF FLOW MODEL

If the cells in sketch (a) are butted against one another forming a continuous cylindrical train moving along the axis with velocity  $\bar{u}_c$ , the velocity profile across the capillary would be as shown qualitatively by the solid curves on the right of the sketch. Thus the velocity of the plasma in the annulus between the cell train and the endothelium varies from  $\bar{u}_c$  adjacent to the cell to zero at the endothelium, and the plasma velocity in the annulus between the endothelium and the true hematolymph barrier varies parabolically and logarithmically between zero on each membrane.

On the other hand, if there were only plasma and no cells in the capillary, the velocity profile within the endothelium plasma would be the Poiseuille parabola shown qualitatively by the dashed line on the right of the sketch, which for a given pressure gradient coincides with the profile between the endothelium and the cell wall (full train).<sup>2</sup>

The actual cell pattern will typically be between the two extremes above; that is, the cells in the train do not form a continuous cylinder - some of the cells in the cylinder are missing and plasma occupies the space between cells. The velocity profile across a cell in the capillary may still be represented by the solid curve on the right of the sketch, and the velocity profile across the plasma where cells are missing would tend toward (but not attain) the parabola shown in the sketch. Since the mass flux along the axis is larger for the parabola than it is for the flattened cell profile, a local adjustment in the flow must be made. The adjustment may be accomplished by the doughnut-shaped vortex observed (ref. 22) between boluses flowing through

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<sup>2</sup>This result that the presence of a core of cells does not disturb the streamlines of the surrounding fluid is a consequence of the force balance (eq. (A2)).

impermeable tubes. Indeed, this mass flux defect is likely the cause of the vortex. The double-walled capillary may permit adjustment by local radial leakage of plasma through the endothelium.<sup>3</sup>

Prothero and Burton (ref. 21) observed experimentally that at large Reynolds numbers the viscous resistance of bolus flow in impermeable tubes was as much as ten times that of Poiseuille flow. However, at small Reynolds numbers (still 500 times that which obtains in the capillary), the bolus flow resistance was only 30 percent greater than that of Poiseuille flow. We suppose that the similarity between the bolus flow of cells and the full train is as good as, and possibly better than, that between bolus flow and Poiseuille flow. For these reasons, and because of the enormous simplification they afford, we neglect any details of the adjustment and, insofar as momentum considerations are concerned, assume that the cells are arranged in a continuous cylindrical train.

However, in our mass conservation considerations (as they relate to hematocrit) we account, in an approximate way, for the fact that cells in the train need not be butted together; some fraction  $(1 - k)$  of the cells of a full train may be missing. In this regard, we need not be too concerned that the velocity profiles across the capillary between cells, obtained from solutions of the momentum equation for a full train, are not strictly correct in detail for the fragmented train. The reason is that we still require the axial mass flux (the integrated velocity profile) to be the same for a cross section of the capillary between cells as it is for one through the cell.

Finally, the results have some features which redeem the model; that is, some of our conclusions about the existence of the extra flow of plasma outside the endothelium are deduced from what the capillary can accomplish under the most favorable condition, the favorable condition being a full train of cells.

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<sup>3</sup>It is possible that this is part of the means by which the plasma annulus is filled outside the endothelium. Thus, as the mixture of cells and plasma entering a capillary adjusts to a single file of cells along the axis, a simultaneous adjustment in the axial mass defect between plasma and cells is accomplished by plasma leaking through the endothelium into the lymph annulus. During that adjustment, cells would move closer together axially, making a more complete train of cells along the axis.

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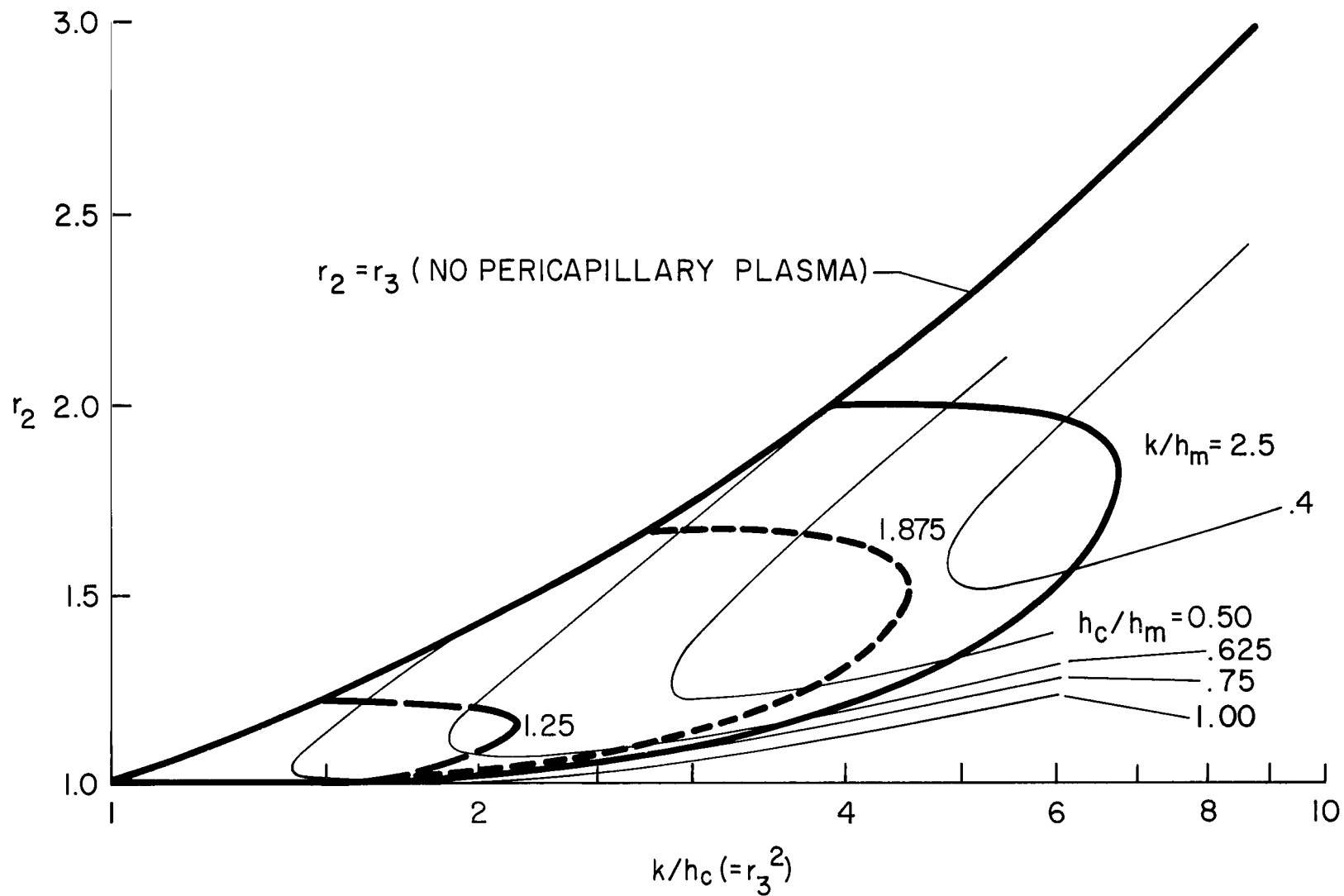


Figure 1.- Roots of equation (1).

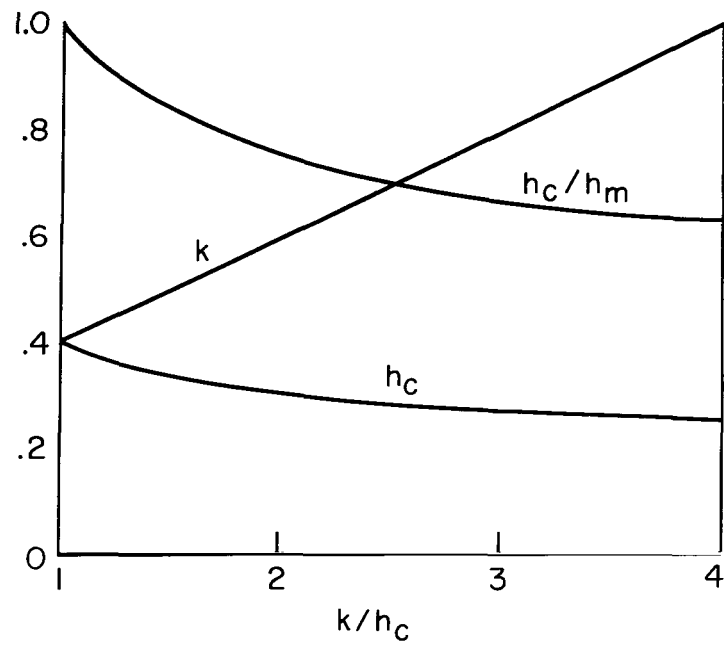


Figure 2.- Relationships for capillary without plasma sleeve outside the endothelium (large blood vessel hematocrit = 0.4).

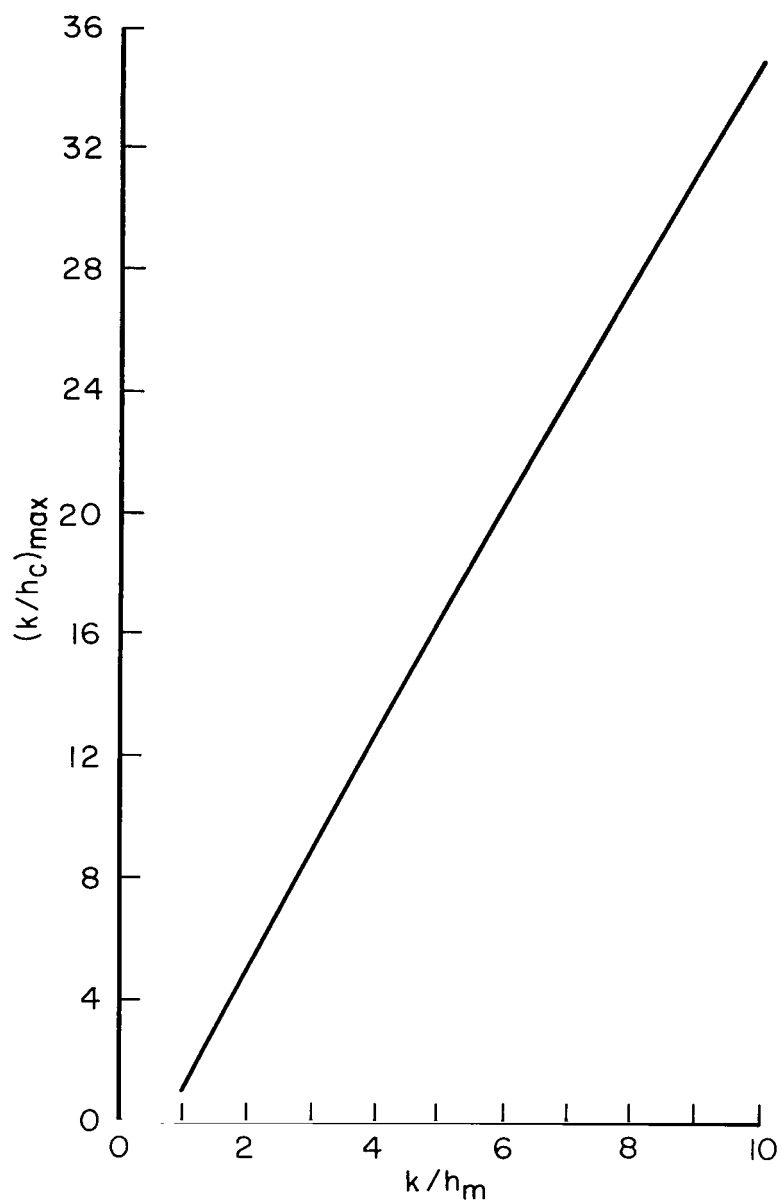


Figure 3.- Maxima in  $k/h_c$  for capillary with pericapillary plasma.

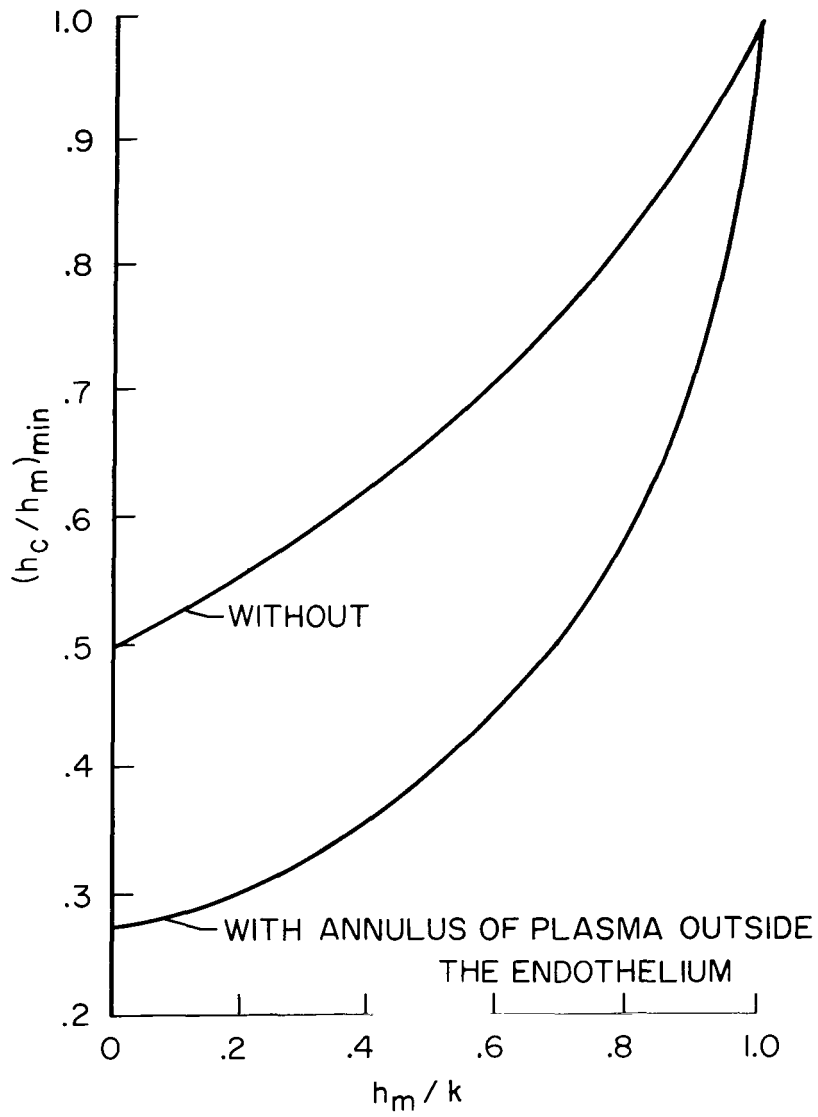


Figure 4.- Minimum ratio of organ hematocrit to large blood vessel hematocrit that can be reconciled by a single capillary.



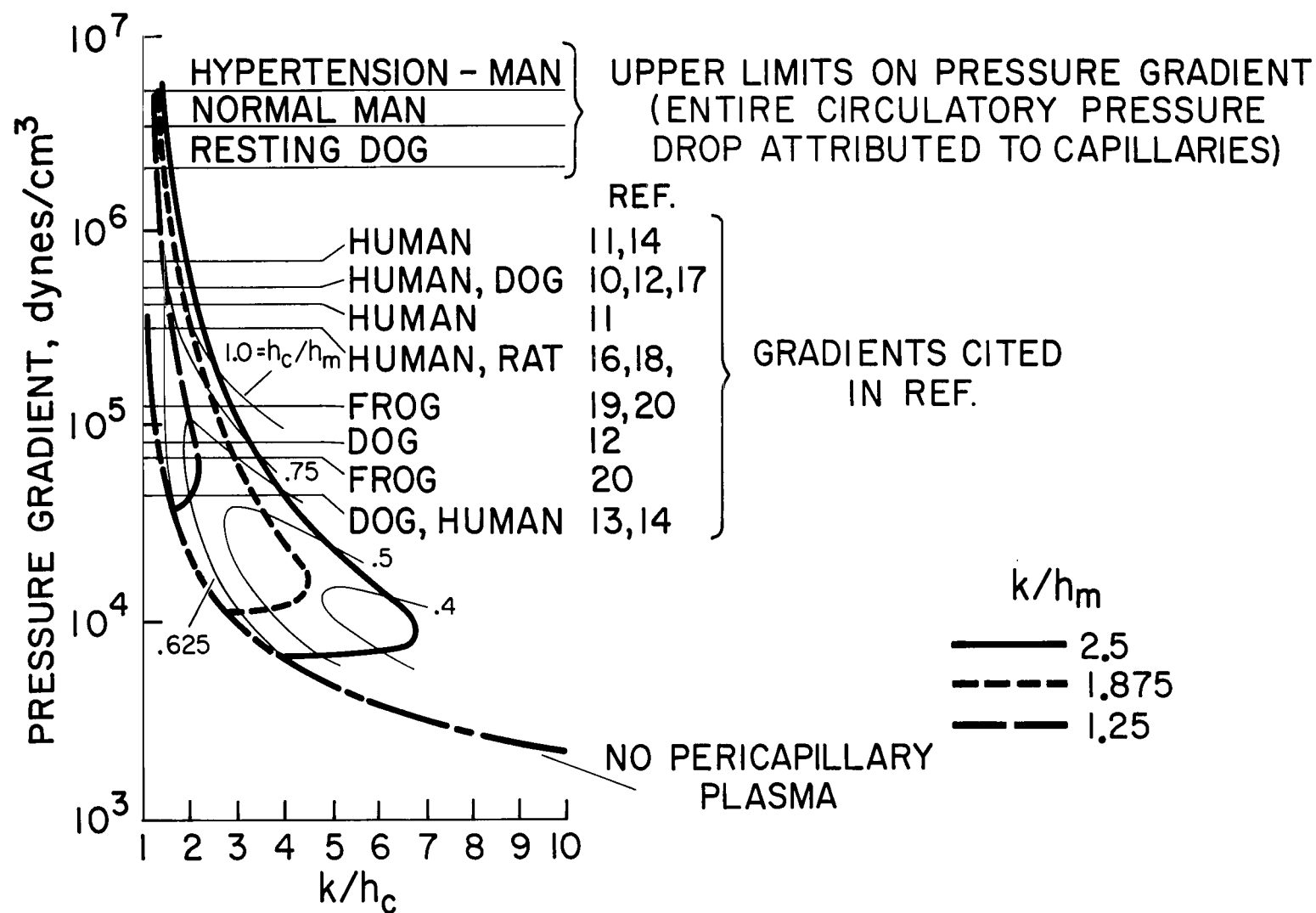


Figure 5.- Pressure gradients corresponding to the three roots of equation (1) compared with those cited in literature ( $\bar{u}_c = 0.4$  mm/sec).

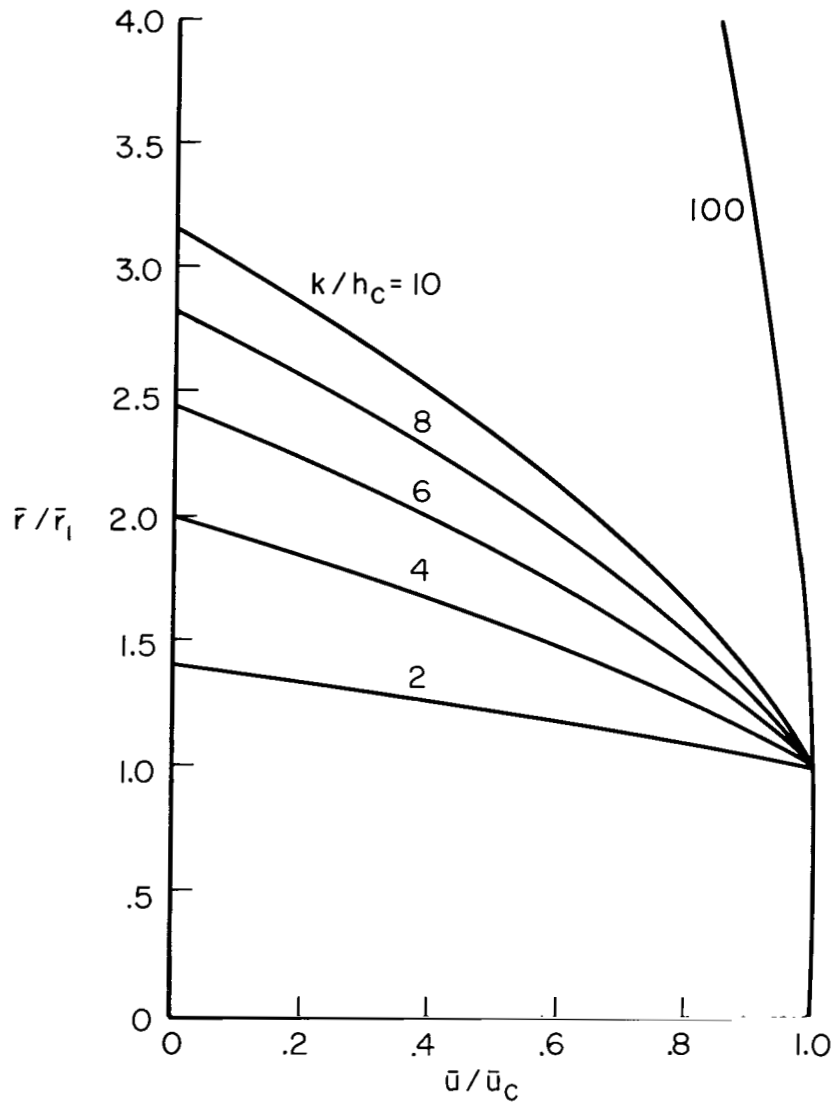
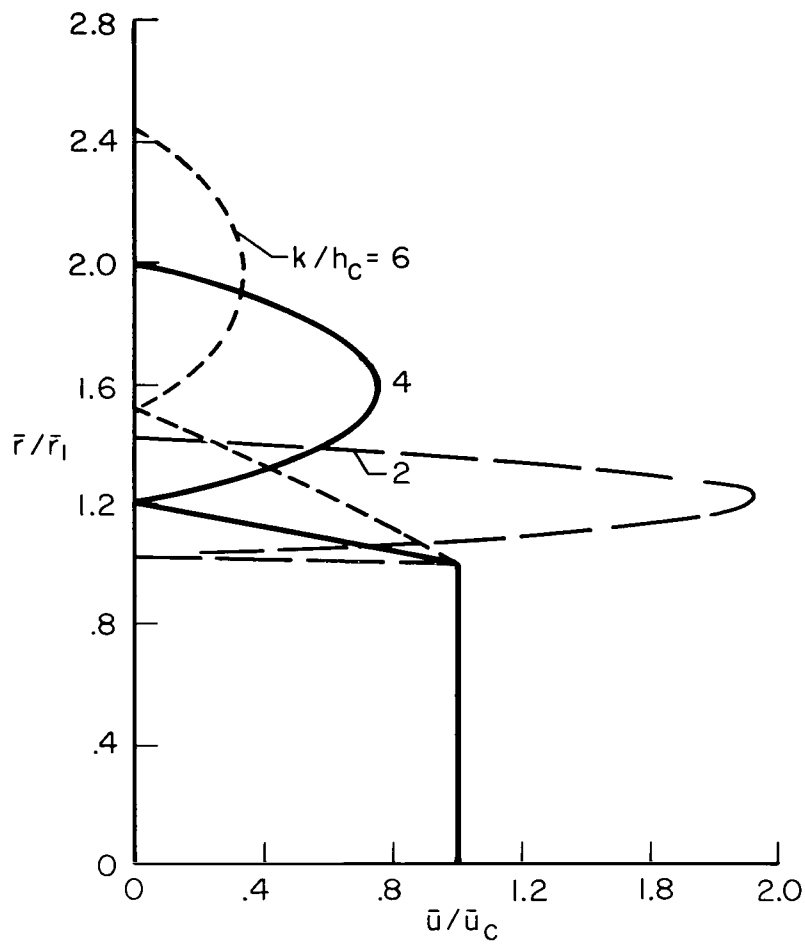
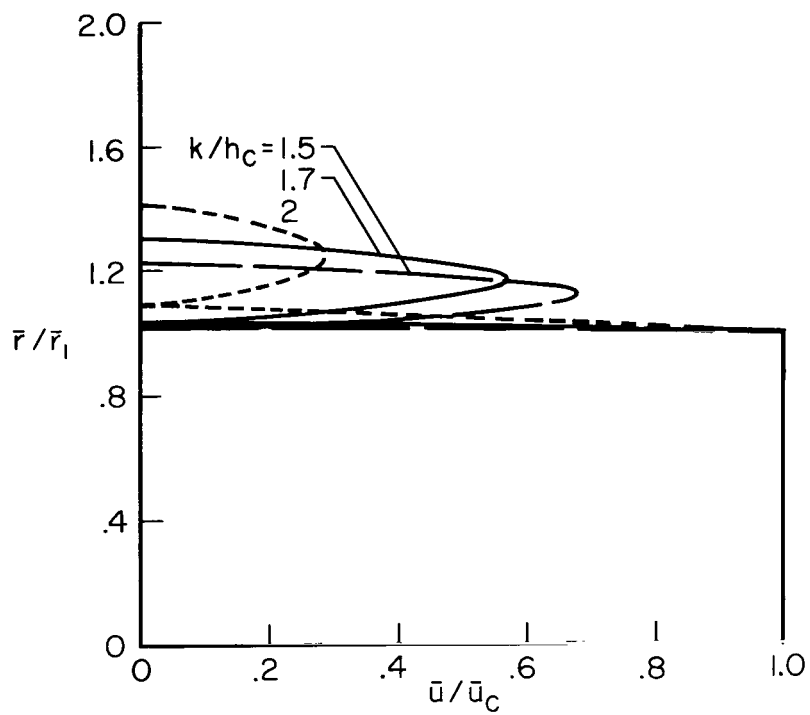


Figure 6.- Velocity profiles - no pericapillary plasma.



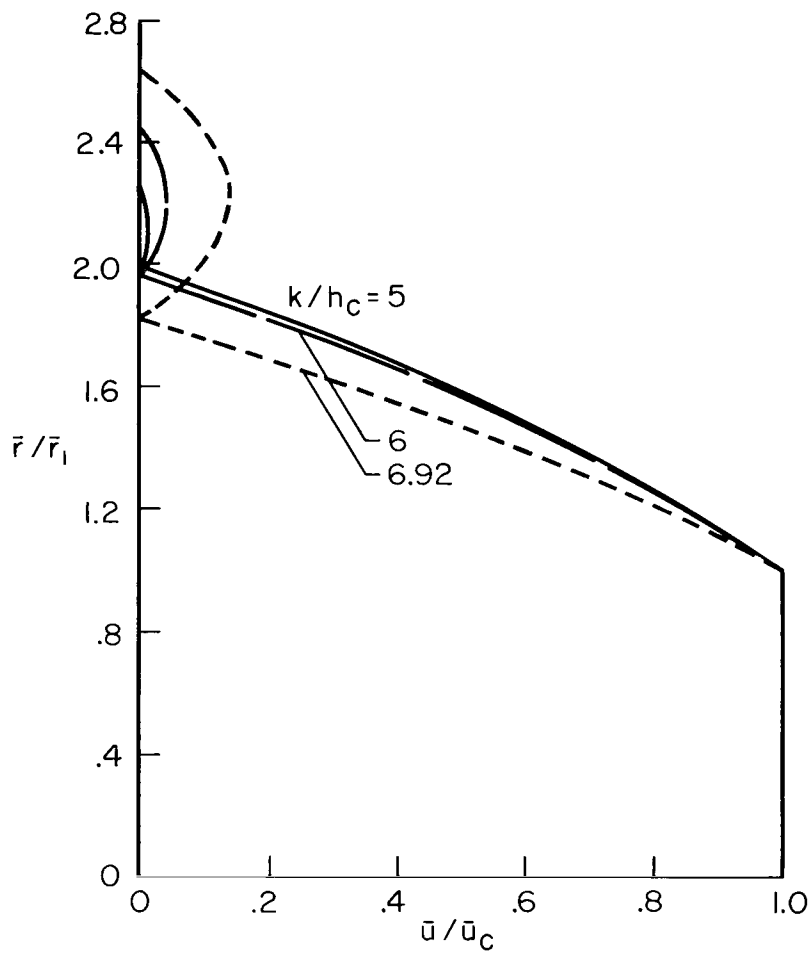
(a)  $k/h_m = 2.5$

Figure 7.- Velocity profiles - lower branch of roots with pericapillary plasma.



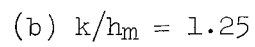
(b)  $k/h_m = 1.25$

Figure 7.- Concluded.



(a)  $k/h_m = 2.5$

Figure 8.- Velocity profiles - upper branch of roots with pericapillary plasma.



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